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INNOVATIONS IN ENVIRONMENTAL SCIENCES RELATED TO CHEMICAL, BIOLOGICAL, RADIOLOGICAL AND NUCLEAR RISKS

Organophosphorus poisoning in animals and enzymatic antidotes

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Abstract
Organophosphorus compounds (OPs) are neurotoxic molecules developed as pesticides and chemical warfare nerve agents (CWNAs). Most of them are covalent inhibitors of acetylcholinesterase (AChE), a key enzyme in nervous systems, and are therefore responsible for numerous poisonings around the world. Many animal models have been studied over the years in order to decipher the toxicity of OPs and to provide insights for therapeutic and decontamination purposes. Environmental impact on wild animal species has been analyzed to understand the consequences of OP uses in agriculture. In complement, various laboratory models, from invertebrates to aquatic organisms, rodents and primates, have been chosen to study chronic and acute toxicity as well as neurobehavioral impact, immune response, developmental disruption, and other pathological signs. Several decontamination approaches were developed to counteract the poisoning effects of OPs. Among these, enzyme-based strategies are particularly attractive as they allow efficient external decontamination without toxicity or environmental impact and may be of interest for treatment. Approaches using bioscavengers for prophylaxis, treatment, and external decontamination are emphasized and their potential is discussed in the light of toxicological observations from various animal models. The relevance of animal models, regarding their cholinergic system and the abundance of naturally protecting enzymes, is also discussed for better extrapolation of results to human.

Keywords Organophosphorus · Pesticides · Chemical warfare nerve agents · Animal models · Decontamination · Enzymatic bio-scavengers

Introduction

Organophosphorus compounds (OPs) are the basis of numerous pesticides and chemical warfare nerve agents (CWNAs) (Szinicz 2005). OP CWNAs can be divided between G agents, gathering CWNAs synthesized by Germany during World War II (tabun (GA), sarin (GB), or soman (GD)), and V agents for the CWNAs developed during the Cold War (VX, VG, VR, among others) which are more toxic than G agents (Hosseini et al. 2016; Costanzi et al. 2018). Since 1993 and effective from 1997, a convention was signed by almost all countries to ban chemical weapons (Organisation for the Prohibition of Chemical Weapons 2005); however, stockpiles still exist and remain to be destroyed. OPs are used as weapons during terrorist attacks like in Japan in 1994–1995 (Masuda et al. 1995; Yanagisawa et al. 2006), in conflicts like in Damascus (Syria) against civilians in august 2013 (Pereira et al. 2014; Patocka 2016) or for Kim Jong-nam's assassination in 2017 in Malaysia (Patočka 2017; Masson and Nachon 2017). Pesticides represent another source of OPs that are more easily available and could be used for terrorist attacks. The use of OP-based pesticides in agriculture and insecticides for indoor disinfestations has been restricted in Europe and the USA, but OPs are still intensively used in other parts of the world especially in developing countries (Eddleston et al. 2002; McKelvey et al. 2013).

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